

(a) contacting in a mixture a target protein with a library of non-oligomeric organic compounds that are each capable of binding covalently to a chemically reactive group on the target protein, thereby forming a target protein-compound conjugate;

(b) analyzing the mixture by mass spectrometry; and

(c) detecting the most abundant target protein-compound conjugate that is formed, and determining the identity of the compound present in said conjugate as the compound having the greatest relative affinity for the target protein,

wherein said compound is a novel ligand for said target protein.

59. (previously added) The method of claim 58 wherein the ligand is less than 1500 daltons in size.

60. (previously canceled)

61. (previously added) The method of claim 58 wherein the ligand is less than 750 daltons in size.

62. (previously added) The method of claim 58 wherein said target protein is a protease.

63. (previously added) The method of claim 58 wherein said target protein is a kinase.

64. (previously added) The method of claim 58 wherein said target protein is a dephosphorylase (phosphatase).

65. (previously added) The method of claim 58 wherein said target protein is a TNF receptor.

66. (previously added) The method of claim 58 wherein said target protein is mdm2 receptor.

67.-80. (previously canceled)

81. (New) The method of claim 58 wherein said chemically reactive group is an -SH group, a protected -SH group or an activated -SH group.

82. (New) The method of claim 81 wherein said -SH group, protected -SH group or activated -SH group is associated with a cysteine residue of said target protein.

83. (New) The method of claim 58 wherein the library comprises at least two members.

84. (New) The method of claim 58 wherein the library comprises at least 25 members.

85. (New) The method of claim 58 wherein the library comprise at lest 100 members.

86. (New) A competition assay comprising:

(a) contacting in a mixture a target protein, a reducing agent, and at least two compounds that are less than 2000 daltons and capable of forming a disulfide bond with the target protein thereby forming a target protein-compound conjugate;

(b) analyzing the mixture by mass spectrometry; and

(c) detecting the most abundant target-protein-compound conjugate that is formed.

87. (New) The assay of claim 96 further comprising determining the identify of the compound that is disulfide bonded to the target protein in the most abundant target protein-compound conjugate that is formed.